VISCERAL ANALGESIA*

A CASE OF MASKED ABDOMINAL CATASTROPHE IN TABES DORSALIS

BY

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A patient with an interesting and unusual complication of tabes dorsalis came under our observation, and because very few similar cases have found their way into the literature, and most of these are of some antiquity, it was thought worthwhile to record and discuss this patient's condition.

It has often been stated that tabes dorsalis may mask serious visceral disease. Power and Murphy (1908–10) have drawn attention to this and Wilson (ed. Bruce, 1940) mentions that tabes " can disrupt nervous pathways so as to produce a visceral analgesia capable of masking serious abdominal disease ". Hanser (1919) published a case of perforated small intestinal ulcer, where a peritonitis of several days' duration was found at autopsy, the patient, a tabetic, having had no sign or symptom (pain, vomiting, tenderness, or rigidity) pointing to this catastrophe. Conner (1910) published a similar case, which was one of perforation of an appendix abscess in a tabetic. Again there was no pain, tenderness, or rigidity ; but fever, vomiting, and a rise in pulse rate were recorded. The author regretted that the splanchnic nerves were not sectioned although the spinal cord was examined. Sternberg (1929) described cases of painless pneumonia and pleurisy, and reviewed the occurrence of analgesia in other organs in tabes.

Roux (1900) dissected the splanchnic nerves from tabetics and from normal patients and attempted to show that these nerves were abnormal in tabes. He made fibre counts and found a numerical difference in the fine fibres. He carried out some experiments to demonstrate analgesia of the stomach in tabes. It was found that pain, accompanying a gastric lesion in those cases with analgesia, radiated to the sides and not to the centre of the abdomen. His work had the support of Dejerine, although Lehmann (1924), who reviewed the occurrence of visceral analgesia in tabes, criticised this work for its incompleteness and the small numbers of cases involved.

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Case Report

History.—The patient was a man aged 59 who attended St. Mary's Hospital, Paddington, from Nov., 1949, until his death in Jan., 1951. He was admitted in November, 1949, complaining of shortness of breath on exertion of a month's duration with paroxysmal nocturnal dyspnoea. There had been difficulty in starting micturition for some months past, and the bladder often became full without the patient noticing it. There was a 10-years' history of lightning pains mainly confined to the legs but also present in the arms. Some unsteadiness of gait was noticed, and he also had numbness of the left leg.

The patient had had syphilis whilst in the army in 1918, when he had received ten injections of arsenicals and mercury, but no follow-up or further treatment. Jaundice had followed the injections. There was a history of rheumatic fever in 1916, consisting of painful polyarthritis and fever.

Examination.—Free aortic incompetence and congestive failure were discovered. A presystolic murmur present at the apex was thought to be an Austin Flint murmur, but mitral stenosis was not excluded. There was some ascites and the liver was enlarged by three fingers' breadth, being firm, regular, and not tender. In the central nervous system there were typical signs of tabes dorsalis with widespread sensory and reflex changes.

An electrocardiogram showed a picture of left ventricular strain.

Blood.—Hb 85 per cent., MCD 7·7 μ, central pallor.

Urine.—A midstream specimen contained pus cells and *B. coli.*

Treatment.—The response of the heart to rest, fluid and salt restrictions, mersalyl, and digitalis was satisfactory. Carbachol was given for a week for overflow incontinence. Two injections of bismuth 0·2 g. were given, followed by procaine penicillin in aluminium monostearate 600,000 units daily for 10 days.

Later Developments.—The patient was discharged, but had to be readmitted within a short time in January,

1950, with the same symptoms. Arrhythmia was noted but the presystolic murmur disappeared temporarily. The electrocardiogram was the same. The cerebrospinal fluid at this time showed five lymphocytes per c.mm., protein 60 mg. per 100 ml., gold curve 4433210, Wassermann reaction +. The pressure was normal and free. After being discharged for a second time, he attended as an out-patient, and received further bismuth.

Final History.—In September, 1950, the patient was readmitted in congestive failure, and painless enlargement of the liver was still noted. Hb 85 per cent., MCHC 33 per cent., MCD 8·2 μ, MCV 95 cu. μ. Plasma proteins normal. Blood urea on several occasions was between 48 and 63 mg. per 100 ml. The extremities were noted to be warm. In spite of treatment the congestive failure did not improve. On October 29 occlusion of the right brachial artery occurred, and intravenous papaverine and intra-arterial 2 per cent. procaine were given. The ascites was tapped in December, 1950. A brief convulsion took place on January 17, 1951, and death occurred on the following day. No localizing central nervous system signs, beside those already present because of tabes, followed the convulsion. The patient's mentality had been clear at all times until the last few days; his appetite had remained good, and one of us watched him eating solid food only one hour before death. With the exception of abdominal discomfort attributed to the congestive failure and which the patient claimed was improved by the mersalyl, there was never any pain and no vomiting or melena was noted. The abdomen was distended and tympanitic but not tender; during the last week the pulse remained steady and the temperature below 99°F.

Post-Mortem Examination (January 18, 1951)

Syphilitic aortitis with atherosclerosis and aortic incompetence were present. The coronary ostia were narrowed. Two cusps of the aortic valve were fused; this was thought to be congenital rather than rheumatic in origin. The other valves were unaffected macroscopically. A large chronic gastric ulcer was found; this had perforated and there was free turbid fluid in the peritoneal cavity. It was considered that the perforation had occurred about 3 days before the autopsy. The ulcer had a vessel at its base which was eroded. An organized thrombus was present in the right brachial artery. The liver was enlarged but not cirrhotic. There was no other significant abnormality.

Pathological Report* on Central Nervous System

Brain.—This was normal in size and no abnormality was seen on external inspection other than a slight opacity of the meninges over the Sylvian fissure and the vertex. After the brain had been cut in a horizontal plane an area of cortical softening about 1 cm. in diameter became visible at the junction of the right insula and the frontal operculum (Fig. 1). The arteries, particularly the basilar and the middle cerebral, were somewhat tortuous and rigid.

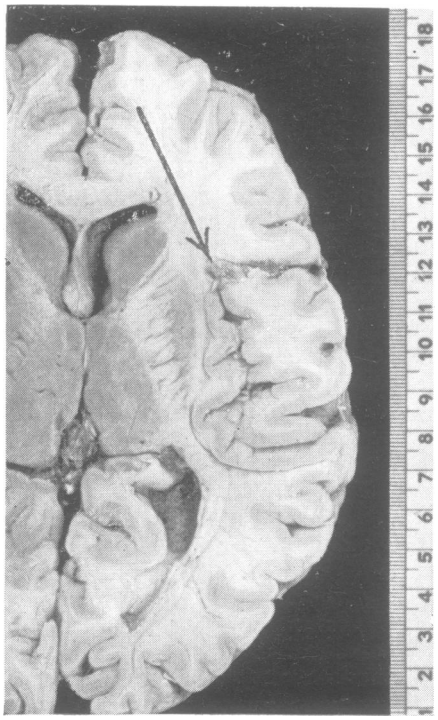

FIG. 1.—Horizontal section of right hemisphere. Cortical softening indicated by arrow.

Coronal sections were taken of the frontal, insular, temporal, and occipital lobes, and of the cerebellum, basal ganglia, and hypothalamus. These blocks, together with the whole of the brain stem and material from representative levels of the spinal cord, were embedded in celloidin. Serial sections were cut of the blocks bearing the area of cortical softening and of the entire brain stem below the level of the 5th nerve nuclei. Frozen and paraffin-embedded sections were also used as required.

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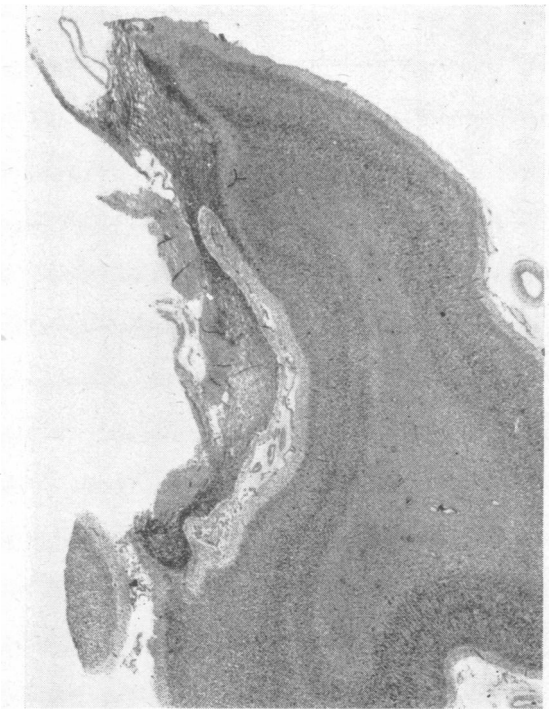

FIG. 2.—Cortical softening as in Fig. 1. Nissl ×7.

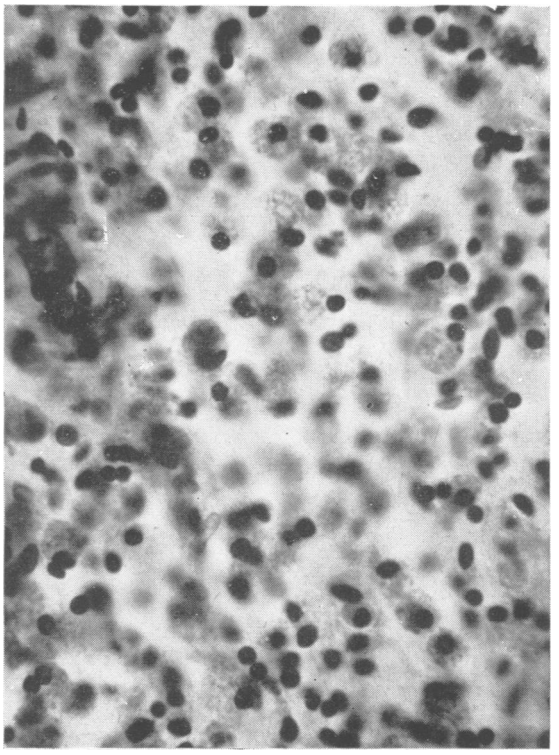

FIG. 3.—Cortical softening. Numerous compound granular corpuscles. Heidenhain ×550.

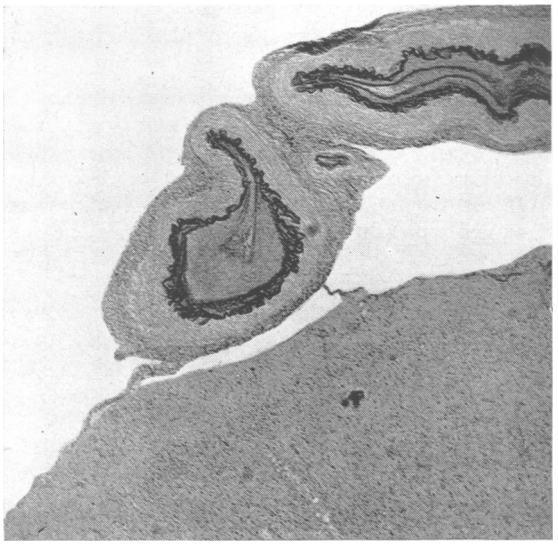

FIG. 4.—Syphilitic endarteritis of one main branch of right middle cerebral artery. Hart Sheridan and carmalum ×25.

Microscopical examination confirmed the presence of an area of softening (Fig. 2) containing a large number of compound granular corpuscles (Fig. 3). There were in addition several smaller areas of complete and incomplete softening within the field of the distribution of the right middle cerebral artery. The branches of that artery showed well-marked endarteritic changes (Fig. 4). The leptomeninges were thickened and contained a moderate quantity of lymphocytes.

There were no localized lesions in the pons or in the medulla, although the basilar artery was also the seat of endarteritis. The nuclei of the 9th, 10th, and 11th cranial nerves were examined with some care and appeared to be normal.

The possibility of paretic changes in the brain was considered but there was no morphological evidence to support this. The nerve cells, it is true, contained an excess of fat, but were not reduced in number. There was, similarly, no perivascular infiltration with lymphocytes and plasma cells. Deposits of iron containing pigment were present in the internal capsule and in the white matter of the cerebellum, but were not sufficiently extensive to suggest general paralysis of the insane.

Senile plaques and neurofibrillary changes were absent.

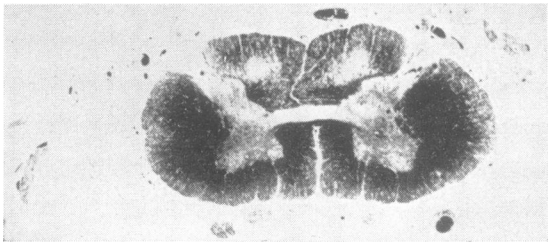

FIG. 5.—Lumbar cord. Heidenhain ×7.

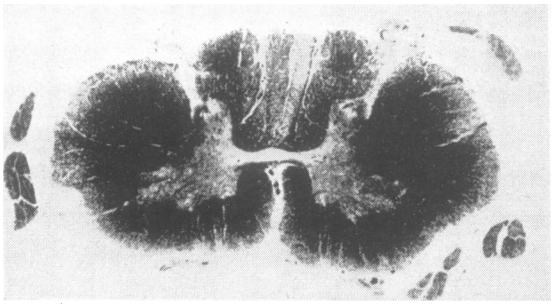

FIG. 6.—Cervical cord. Heidenhain ×7.

Spinal Cord.—Wasting of the posterior columns of the spinal cord could be seen on macroscopic inspection. Demyelination was apparent in suitably stained sections and affected particularly the middle third of the posterior columns in the lumbar cord (Fig. 5), and the fasciculus gracilis at the thoracic and cervical levels (Fig. 6). Fibrous gliosis was present in the grey commissure of the cord and in some of the areas corresponding with the demyelination. A moderate degree of demyelination was also present in the marginal zone throughout the entire length of the spinal cord.

The nerve cells in the anterior and posterior horns contained a considerable excess of fat, but were not appreciably reduced in number. The soft meninges over the cord were greatly thickened (Fig. 7) and contained scattered mononuclear cells, most of which were lymphocytes.

Nerve Roots and Ganglia.—The nerve roots between the dura and the posterior root ganglia —the *nerve radiculaire* of Nageotte—showed small areas of scar tissue. The membranes covering the nerve roots were greatly thickened and the prolongation of the dura could not be distinguished from the arachnoid.

The nerve cells in the posterior root ganglia contained an excess of fat. Minute granules of brown pigment, reminiscent of that seen in the heart fibres in brown atrophy, were present in the

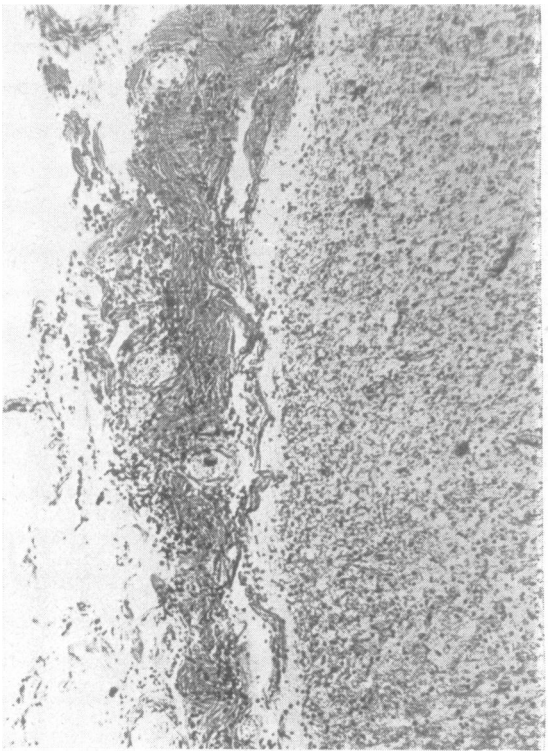

FIG. 7.—Meninges of spinal cord. Haematoxylin and Van Gieson ×125.

spindle-shaped cells filling the spaces between the nerve cells. Some of the latter were irregular in outline and contained vacuoles and fenestrations in their cytoplasm. These changes, however, were difficult to interpret, since similar findings are frequently present in material from normal cases.

Discussion of Pathology

The structural features in this instance were characteristic of a moderately-advanced case of tabes dorsalis associated with meningo-vascular syphilis. There was, as mentioned above, no evidence of paresis.

The present case throws no new light on the situation of the pathway for visceral sensation. The widespread nature of the lesions, even allowing for the failure to examine the splanchnic nerves, the sympathetic ganglia, and the vagi, could have accounted for the interruption of the fibres conveying visceral sensation at several different levels.

Visceral Pain Mechanisms

Visceral pain can apparently be conveyed by three mechanisms (Bockus, 1950). (1) True visceral

pain which occurs after the appropriate stimulus is applied, such as distension of a hollow viscus setting up spasm, stretching of the capsule of a solid organ, inflammation in an organ setting up spasm or by irritation of its serous layer, or anoxaemia. The pain is protopathic in type, that is, diffuse, deep, poorly localized, and usually felt in the midline. Its path of conduction is by way of the sympathetic nervous system. In the case of the stomach this is *via* the greater splanchnic nerves with root values T 6th to 9th, mainly 7th and 8th. Bentley and Smithwick (1940), who produced visceral pain by distending a swallowed balloon in the upper jejunum in hypertensive patients before sympathectomy, found that this pain was abolished on the side of the splanchnicectomy.

(2) Referred pain, the mechanism of which is still disputed and the validity of which is still in doubt (Morley, 1929). Sensory impulses, travelling by way of the sympathetic nerves to the spinal cord, are communicated *via* the sensory nerves of the same cord segment to a somatic dermatome. The most prominent theories are those of Mackenzie (1893) and Ross (1888), who believed that an irritable focus is set up in the cord by severe stimulation of the sympathetic, and of Hinsey and Phillips (1940), who assume that both visceral and somatic afferents are stimulated and affect a common pool of secondary neurones in the cord and that the rules of summation and inhibition are applicable. Referred pain is usually epicritic ; that is, sharp, immediate, and well localized, and probably requires a comparatively larger visceral stimulus for its production. Thus its extent will depend upon strength of stimulus and lowering of pain threshold.

(3) The third mechanism accounting for pain originating from stimuli within the abdomen travels purely by somatic nerves. The nerve endings lie in the parietal peritoneum, and fibres may extend into the root of the mesentery and the posterior parieties. Morley (1937) named it the " peritoneo-cutaneous reflex ". The pain is communicated from peritoneal nerve endings *via* the corresponding somatic fibres to skin areas of the abdomen. Similarly pain in the neck and inside of the arm, and in the trapezius area, may follow stimulation of the phrenic nerve endings in the centre of the diaphragm on its under side. In the abdomen it is associated with guarding of the muscles and rigidity. The pain can be severe and sharply localized.

Cohen (1946) suggests that pain nerve endings send a regular stream of impulses to the central nervous system, which are normally subthreshold ; an increase in the pain impulses in a viscus will enter consciousness if they are sufficiently intense in themselves, or are reinforced by impulses normally arising from the pain nerve endings in homosegmental somatic structures. This explains why a local anaesthetic which blocks somatic impulses may abolish visceral pain of the same segment. If, however, the viscus impulses alone are adequate to overstep the threshold, the resulting pain may be diminished but not abolished by anaesthetization of the peripheral nerves of the segment in question.

Little is known of any sensory function of the abdominal vagus. Brain (1951) states that pain can travel *via* sympathetic or parasympathetic nerves ; referred pain by way of the vagus being referred to the trigeminal and upper cervical sensory areas.

Visceral pain is probably projected to the frontal lobes by the hypothalamus, the latter standing in the same relation as the thalamus stands to somatic pain (Fulton, 1949). However this is not in agreement with the experimental studies of Amassian (1951), who considers that the thalamus plays the major role in the pathway of visceral as of somatic impulses.

The path taken by impulses travelling up the afferent sympathetic fibres is in non-medullated fibres entering the cord through the dorsal roots, whence the pathway according to Davis and others (1929) lies in the lateral funiculus near the posterior horn, or according to Spiegel and Bernis (1925) the tracts lie in the antero-lateral columns. The fibres cross at various levels, and the impulses may ascend by short spinal arcs in both ipsilateral and contralateral tracts (Kuntz, 1946).

The evidence for any such suggested pathways of visceral sensation is not conclusive. It has recently been shown by Amassian (1951) that visceral sensation, which he studied by electrical methods in rabbits, dogs, cats, and one monkey, is conducted in the posterior columns of the cord. It is not certain, of course, that the visceral sensation fibres in man are confined to any one column of the cord. If some or most of these fibres were, however, to be located in the posterior columns, then a clinical study in cases of tabes dorsalis might throw some light on the applicability of these results to man. One's clinical impression is that visceral analgesia is not as common as these studies might lead one to expect.

For surgical relief of abdominal visceral pain, extensive procedures may thus have to be undertaken, such as transverse section of the white matter of the cord, extensive and bilateral thoracic posterior rhizotomy, or frontal lobotomy.

Experimental production of pain in the alimentary tract by means of balloons showed that visceral

pain was more diffuse with radiation into wider areas after sympathectomy, and that the pain threshold was raised. Regeneration of pathways did not occur (Bingham and others, 1950), and these workers noted that tenderness may persist in the absence of pain in a patient who has had a sympathectomy; they noted that "peritoneo-cutaneous reflex" tenderness was abolished by intercostal nerve block, and also that the tenderness due to direct pressure on a diseased organ was absent after splanchnic nerve section but not after anaesthetizing the abdominal wall.

Discussion

In this patient it is thought that the true visceral pain pathway from the stomach was interrupted by the syphilitic process, thus explaining the painless course of a large gastric ulcer over the years. Had these been the only nerve fibres affected, however, pain *via* the somatic nerves, partly in referred pain and wholly in Morley's peritoneo-cutaneous reflex, would have emerged at the time of perforation and subsequent peritonitis. One must therefore assume an interruption of somatic nerve paths for visceral pain. It is significant that the whole trunk was insensitive to pin-prick and that the patient had also an insensitive bladder. Bockus (1950) maintains that the incidence of peptic ulcer in neurosyphilis is no greater than that in the population as a whole and quotes Crohn's figure of 8 per cent. That peptic ulcer may be of a trophic nature is likewise not as widely believed as formerly (Hunt and Lisa, quoted by Stokes and others, 1944).

Alvarez (1931), discussing splanchnic nerve section for the relief of abdominal pain especially in gastrojejunal ulcers, gives warning of the danger of subsequent silent perforation. He then quotes animal experiments in which section of the splanchnics was followed by gastric ulcers; this is of interest as it may have some bearing on our case.

It would appear that for a painless abdominal catastrophe to occur, both autonomic and somatic channels must be affected bilaterally. In the conditions in which severe pain is a feature this abrogation of all sensory warning is rarely anything but distressing; the improvement of a post-herpetic neuralgia in a progressing tabes is an example of the less dangerous effects. The present case is an example of the possible dangers, and one would like to know what the effects of such widespread sensory changes would be on the recognition of such conditions as myocardial infarction.

Autonomic (mainly sympathetic) irritation is thought to be the largest factor in the production of crises in tabes. Perhaps it is significant that in such a well-developed case as that under discussion there was no gastric crisis, and one wonders whether sympathetic nerve-blocking agents might not be a useful measure in dealing with intractable visceral crises in neurosyphilis.

Sympathectomy and rhizotomy are now not undertaken for the relief of tabetic pains or crises, but sympathectomy is performed in arterial disease, hypertension, hyperhidrosis, causalgia, and angina. This should not mask an abdominal catastrophe or other visceral cause for severe pain, since only one channel for pain propagation is blocked. However, in the early stages of visceral disease when low-threshold pain impulses are produced, which are transmitted by the sympathetic system, warning of the disease might not be forthcoming. Not until stronger impulses from extension of the disease process had arisen would the referred pain mechanism be initiated, and unequivocal evidence might not appear until the parietal serous layer was involved. Bingham and others (1950) have analysed case histories of patients with peptic ulcer, biliary tract disease, and dysmenorrhoea on whom sympathectomy had been performed, and they describe the effect of the operation on the natural history of these diseases.

Summary

A case is described of silent gastric perforation in a tabetic. The literature of this subject is briefly reviewed. The mechanisms of visceral pain of particular interest are recapitulated and the occurrence of visceral analgesia discussed.

It is felt that cases of tabes dorsalis with extensive, bilateral, sensory loss should be investigated with special regard to visceral disease since the progress of such a condition may be silent.

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